REMARKS

I. STATUS OF THE APPLICATION

Claims 1–105 were cancelled, and claims 106–191 were added in the Amendment and Request for Continued Examination after Board Decision of July 25, 2006. Claim 126 was cancelled, and claims 106, 125, 134, 143, 144, 149, 160, 176 and 186–189 were amended in the Amendment and Response to the Final Office Action of December 11, 2007. Therefore, claims 106–125, and 127–191, are currently pending.

In the Office Action of September 11, 2007 there are 5 rejections. The currently pending rejections are:

1. Claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al.* (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia").

2. Claims 151-160, 187-188, and 190 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al.* (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter

"Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of Lapointe et al. (US 6,678,669, January, 2004) (hereinafter "LaPointe").

3. Claim 185 is rejected under under 35 U.S.C. 103(a) as allegedly being unpatentable over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al*. (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of Lyamichev et al. (Nature Biotechnology, Vol. 17, pages 292-296, March, 1999) (hereinafter "Lyamichev").

4. Claims 125 and 134 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Miller (Anesthesia, Vol. 2, pages 1323-1333, 1981) (hereinafter "Miller") in view of Quane *et al.* (Human Molecular Genetics, Vol 3, No. 3, page 471-476, 1994) (hereinafter "Quane") or Acta Anaesthesiologica Scandinavica (Vol 39, page 139-141, 1995) (hereinafter "Acta") and La Du (Cellular and Molecular Neurobiology, Vol 11, No. 1, page 79-89, 1991) (hereinafter "La Du") or Pharmacogenetics (Chapter 4, pages 309-326, IDS #201) (hereinafter "Pharmacogenetics") and Evans *et al.* (Science, Vol 286, pages 487-491, October 1999) (hereinafter "Evans') or Poort *et al.* (Blood, Vol 88, No 10, page 3698-3703, 1996) (hereinafter "Poort'), and further in view of Hoon *et al.* (US Pat. 6,057,105, May 2, 2000) (hereinafter "Hoon") and Hacia (Nature Genetics Supplement, Vol. 21, pages 42-47, January, 1999) (hereinafter "Hacia") as applied to claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 above, and further in view of the specification (Tables 1-4).

5. Claims 125, 134, 160 and 186 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention.

II. STATUS OF THE REJECTIONS

II.A. Miller in view of Quane or Acta and La Du or Pharmacogenetics and Evans or Poort, and further in view of Hoon and Hacia Does Not Render the Claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 Obvious

The Examiner has rejected claims 106 – 124, 127-133, 135-150, 161-186, 189 and 191 under 35 U.S.C. 103(a) as allegedly being unpatentable over Miller in view of Quane

or Acta and La Du or Pharmacogenetics and Evans or Poort, and further in view of Hoon and Hacia.

A *prima facie* case of obviousness requires the Examiner to cite to a reference which a) discloses all the elements of the claimed invention, b) suggests or motivates one of ordinary skill in the art to combine the claim elements to yield the claimed invention, and c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements negates a finding of a *prima facie* case and, without more, entitles the Applicant to allowance of the claims in issue. (MPEP)

The Applicant submits that: a) none of the Examiner's references, alone or in combination, disclose all elements of the claimed invention; and b) the Examiner has failed to provide a suggestion or motivation to combine the elements to yield the claimed invention so as to evidence obviousness.

II.A.1. Missing Elements in Miller in view of Quane or Acta and La Du or Pharmacogenetics and Evans or Poort, and further in view of Hoon and Hacia

The Applicant submits that the Examiner's combination of references fails to disclose not just one, but multiple elements of the claimed invention. Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims.

In the Office Action of September 11, 2007 the Examiner concedes that Miller does not specifically teach analyzing blood prior to surgery for "two or more known genetic markers associated with two or more conditions." (Office Action of September 11, 2007, page 2.) The Applicant points out that none of the Examiner's additional 8 references alone or in combination remedy the defects of these missing elements, nor has the Examiner indicated where these missing elements are to be found in the Examiner's combination.

Accordingly, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.a. The Examiner's combination of references is missing the elements of selecting a perioperative course of action based on information from a perioperative genomic profile, and performing a surgical procedure (Claim 106)

In the Office Action of September 11, 2007 the Examiner argues:

"The response asserts Claim 106 requires selecting a perioperative course of action based upon information from the genomic profile. The Examiner fully agrees. However, once the ordinary artisan realized a patient was predisposed to have an adverse reaction to anesthesia or other condition, the ordinary artisan would have selected a course of action consistent with this discovery and acted appropriate." (Office Action of September 11, 2007, page 12.)

And:

"Doctors are subject to liability. In the event that the skilled doctor did not heed the warnings of a genetic test performed, liability would attach. Thus, the ordinary artisan would have been motivated to have taken what was determined and discovered from the genetic profile and used the information in a prudent manner to avoid any complications that may exist given information generated from the genetic analysis." (Office Action of September 11, 2007, page 12.) (Emphasis added.)

The Applicant respectfully disagrees. First, the Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Second, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do. This does not legally compensate for a need to show the element in the evidence provided with the rejection. Third, the Examiner's speculations concerning

professional liability do not provide the missing elements, or remedy the rejection's defects.

The Applicant notes that the element "selecting a perioperative course of action based on information from said genomic profile" is a method step that limits the scope of claim 106. Claim 106 is thereby limited to a process that includes selecting a perioperative course of action based on the results of the perioperative genomic profile, and is in accord with the Decision on Appeal's holding regarding claim language providing a patentable step in a method claim (Ex parte KIRK HOGAN, page 5). In the Office Action of September 11, 2007 the Examiner has failed to point out where in the Examiner's cited references this element based on information from a perioperative genomic profile is to be found.

Moreover, in the Office Action of September 11, 2007 the Examiner again mixes selecting a perioperative course of action with selecting a genomic profile ("It would have been obvious once the genomic profile was selected . . ." (Office Action of September 11, 2007, page 12.)). Only by knowing the specific results of the perioperative genomic profile in a specific patient is it possible to select a specific perioperative course of action on the basis of the specific results. It is not possible, as the Examiner argues, to select a perioperative course of action merely by selecting a genomic profile. Nor has the Examiner responded to these facts in the Office Action of September 11, 2007.

As well, the element "performing said surgical procedure wherein said perioperative course of action is used by at least one of the group consisting of an anesthesiologist, a nurse, and a surgeon" is a method step that limits the scope of claim 106. Claim 106 is thereby limited to a process that includes performing a surgical procedure based on the results of the perioperative genomic profile, and is in accord with the Decision on Appeal's holding regarding claim language providing a patentable step in a method claim (Ex parte KIRK HOGAN, page 5). The Examiner's cited references provide no guidance regarding which two or more nucleic acid markers in two or more genes associated with two or more conditions may be used to carry out a surgical procedure correctly. Nor do the Examiner's cited references provide guidance to the anesthesiologist, nurse, or surgeon to balance information from the components of the

perioperative genomic profile. In the Office Action of September 11, 2007 the Examiner has failed to indicate where in the Examiner's combination of references these elements are to be found.

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 106, or of claims that are dependent thereupon. Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.b. The Examiner's combination of references is missing the element of a perioperative course of action based on information from a perioperative genomic profile for a first surgical procedure (Claim 107)

In the Office Action of September 11, 2007 the Examiner notes:

> "The response argues that the combination of references is missing the limitation that a perioperative course of action is for the first surgical procedure for the subject (claim 107). This argument has been reviewed but is not persuasive. The ordinary artisan would be motivated to screen patients for any and all surgeries to ensure precautions are taken to prevent any complications." (Office Action of September 11, 2007, page 13.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 107. The element of a

perioperative course of action based on information from a perioperative genomic profile for a first surgical procedure does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner's citation of the Quane reference merely suggests testing for a single disorder in a single gene after a patient has had a prior complication during a surgical procedure. The Examiner has not indicated where the element "for a first surgical procedure" is to be located in the Examiner's cited references. Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims.

In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.c. The Examiner's combination of references is missing the element of a course of action based on information from a perioperative genomic profile for administration of anesthesia during a medical procedure (Claims 117, 168)

In the Office Action of September 11, 2007 the Examiner notes:

> "The response argues that the combination of references is missing the limitation that the course of action comprises administration of anesthesia during a medical procedure. This argument has been reviewed but is not persuasive. The Quane reference teaches that "once an individual is diagnosed as being susceptible to MH, the anaesthetics which trigger this syndrome can be avoided." (Office Action of September 11, 2007, page 13.)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 117 and 168. The element of a course of action based on information from a perioperative genomic profile for administration of anesthesia during a medical procedure does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner's citation of the Quane reference merely suggests testing for a single disorder in a single

gene. Quane does not teach or suggest the element of a course of action based on information from a perioperative genomic profile. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.d. The Examiner's combination of references is missing the element of a perioperative genomic profile comprising a presymptomatic risk (Claim 120)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 120. The element of a perioperative genomic profile comprising a presymptomatic risk does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The response argues that the combination of references is missing the limitation that the genomic profile comprises information comprising presympotomatic risk. This arugment has been reviewed but is not persuasive. The ordinary artisan would be motivated to screen patients for any and all surgeries to ensure precautions are taken to prevent any complications before signs are shown. The ordinary artisan would be motivated to test for MH prior to triggering a response that would cause death." (Office Action of September 11, 2007, page 14.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing element

in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.e. The Examiner's combination of references is missing the element of a perioperative genomic profile comprising information for differential diagnosis of co-existing diseases (Claim 121)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 121. The element of a perioperative genomic profile comprising information for differential diagnosis of co-existing diseases does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The ordinary artisan would be motivated to diagnose the specific condition that is associated with poor response to anesthesia." (Office Action of September 11, 2007, page 14.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.f. The Examiner's combination of references is missing the element of selecting a surgical procedure treatment course of action (Claim 127)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 127, or of claims that are dependent thereupon. The element of selecting a surgical procedure treatment course of action does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "Doctors are subject to liability. In the event that the skilled doctor did not heed the warnings of a genetic test performed, liability would attach. Thus, the ordinary artisan would have been motivated to have taken what was determined and discovered form the genetic profile and used the information in a prudent manner to avoid any complications that may exist give the information generated from the genetic analysis." (Office Action of September 11, 2007, page 15.) (Emphasis added.)

The Applicant respectfully disagrees. First, the Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Second, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do. Third, the Examiner's speculations concerning professional liability do not provide the missing elements, or remedy the rejection's defects.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.g. The Examiner's combination of references is missing the element of a perioperative genomic profile consisting of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, and TNFα (Claim 134)

The Applicant notes that claim 134 is withdrawn from the present rejection. Nevertheless, the Examiner notes:

> "This argument has been reviewed and the claim is rejected below in view of the Specification." (Office Action of September 11, 2007, page 15.)

II.A.1.h. The Examiner's combination of references is missing the element of non-invasive surgery (Claims 139, 179)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 139 and 179. The element of non-invasive surgery does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The ordinary artisan would be motivated to screen patients for any and all surgeries to ensure precautions are taken to prevent any complications before signs are shown. The ordinary artisan would be motivated to test for MH prior to triggering a response that would cause death." (Office Action of September 11, 2007, page 15.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the

Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.i. The Examiner's combination of references is missing the element of selection of monitoring procedures based on the results of a perioperative genomic profile (Claim 148, 175)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 148 and 175. The element of selection of monitoring procedures based on the results of a perioperative genomic profile does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The response asserts that the combination of elements fails to teach selection of monitoring procedures based upon the profile. This argument has been reviewed but deemed not persuasive. The ordinary artisan would have been motivated to have monitored procedures." (Office Action of September 11, 2007, page 16.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.j. The Examiner's combination of references is missing the element of obtaining consent from a perioperative subject to assay a sample for genetic variations (Claim 149)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claim 149, or of claims that are dependent thereupon. The element of obtaining consent from a perioperative subject to assay a sample for genetic variations does not appear in Miller. The Examiner has not indicated where this element is to be located in the Miller.

In the Office Action of September 11, 2007 the Examiner argues:

> "The response asserts that the combination of references is missing the element of obtaining consent from a perioperative subject to assay a sample for genetic variation (claim 149). Despite Miller teaching obtaining consent for perioperative tests and analysis, the response asserts that this is not consent for a genetic variation test. This argument has been reviewed but is not persuasive. The ordinary artisan would have been motivated to have obtained consent for ANY procedure in the medical field, as is routine and customary in the field to avoid malpractice allegations." (Office Action of September 11, 2007, page 16.) (Underlining added.)

The Applicant respectfully disagrees. First, the Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Second, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been

motivated to do. Third, the Examiner's speculations concerning professional liability do not provide the missing elements, or remedy the rejection's defects.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.k. The Examiner's combination of references is missing the element of distributing the results of a patient's perioperative genomic profile according to the patient's preference wherein the distributing is selected from the group consisting of destroying the results, saving the results for future access by the patient, saving the results for future access by a clinician, and donating the results for research (Claims 149, 189)

The Applicant notes that the element of "distributing said results of said patient's said genomic profile according to said patient's preference wherein said distributing is selected from the group consisting of destroying said results, saving said results for future access by said patient, saving said results for future access by said clinician, and donating said results for research;" does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where in the Examiner's cited references "distributing said results of said patient's said genomic profile according to said patient's preference" is to be located.

In the Office Action of September 11, 2007 the Examiner notes:

> "It is not apparent what other choices were available to the patient. Thus, the ordinary artisan would have been motivated to have done one of these two actions." (Office Action of September 11, 2007, page 17.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing

elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.l. The Examiner's combination of references is missing the element of distributing the patient's sample according to the patient's preference wherein the distributing is selected from the group consisting of destroying the sample, saving the sample for future access, and donating the sample for research (Claims 149, 189)

The Applicant notes that the element of "distributing said patient's said sample according to said patient's preference wherein said distributing is selected from the group consisting of destroying said sample, saving said sample for future access, and donating said sample for research."does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where in the Examiner's cited references "distributing said patient's said sample according to said patient's preference" is to be located.

In the Office Action of September 11, 2007 the Examiner notes:

> "The ordinary artisan would have either destroying the sample or saving the sample. It is not apparent what other choices were available to the patient. Thus the ordinary artisan would have been motivated to have done one of these two actions." (Office Action of September 11, 2007, page 17.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the

Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.m. The Examiner's combination of references is missing the element of a computer program comprising instructions which direct a processor to analyze results of a perioperative genomic profile (Claim 150)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 150. The element of a computer program comprising instructions which direct a processor to analyze results of a perioperative genomic profile does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The response asserts that the combination of references is missing the element of a computer program comprising instructions which direct a processor to analyze results of a perioperative genomic profile. This argument has been reviewed but is not persuasive. Hacia teaches mutations are detected by a minisequencing assay using an algorithm." (Office Action of September 11, 2007, page 18.)

The Applicant points out that Hacia fails to remedy the defects of the Examiners's rejection. For example, Hacia does not teach or suggest a perioperative genomic profile. As well, Hacia does not teach or suggest a processor to analyze results of a perioperative genomic profile. Moreover, Hacia does not teach or suggest a computer program comprising instructions which direct a processor to analyze results of a perioperative genomic profile. In the Office Action of September 11, 2007 the Examiner has not indicated where these elements that are missing in the Examiner's combination of

references are to be found in Hacia, or in any of the other references cited by the Examiner alone or in combination.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.o. The Examiner's combination of references is missing the element of an assay comprising structure-specific cleavage of oligonucleotide probes (Claim 185)

In the Office Action of September 11, 2007 the Examiner notes:

"The response asserts that combination fails to teach certain elements. In view of the newly presented rejection below over Lyamichev, these arguments are moot." (Office Action of Septembe 11, 2007, page 18.)

Accordingly, claim 185 is addressed below.

II.A.1.p. The Examiner's combination of references is missing the element of providing a kit comprising a computer program on a computer readable medium comprising instructions which direct a processor to analyze data derived from use of reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, the subject being a patient scheduled for a surgical procedure that has not yet completed the surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS,* and *TNFα* so as to generate a genomic profile for use in selecting a perioperative course of action for the subject (Claim 186)

In the Office Action of September 11, 2007 the Examiner notes:

> "The response asserts that the combination of references is missing the element of a kit comprising a computer program." (Office Action of September 11, 2007, page 18.)

The Applicant asserts that the Examiner has misread claim 186. Contrary to the Examiner's characterization claim 186 recites a kit comprising a computer program on a computer readable medium comprising instructions which direct a processor to analyze data derived from use of reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, the subject being a patient scheduled for a surgical procedure that has not yet completed the surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS,* and *TNF*α so as to generate a genomic profile for use in selecting a perioperative course of action for the subject. The Applicant notes that Hacia does not teach or suggest such a computer program on a computer readable medium, nor does such a computer program on a computer readable medium appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, or Hoon alone or in combination. In the Office Action of September 11, 2007 the Examiner has not indicated where this element is to be located in the Examiner's cited references.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.u. The Examiner's combination of references is missing the element of generating a perioperative genomic profile with the kit of Claim 186 (Claim 186)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 186. The element of generating a perioperative genomic profile with the kit of Claim 186 does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

> "The response asserts that the combination of references is missing the element of teaching of a kit for generating a perioperative genomic profile. . . . The providing of the computer and algorithm meets the requirement of a kit. A kit, without more, is merely a composition of reagents." (Office Action of September 11, 2007, page 19.)

The Applicant asserts that the Examiner has misread claim 186. Claim 186 is a claim dependent upon the method claim 149. The element "generating said genomic profile with said kit" is a step that limits the scope of claim 149 in that it dictates the parameters of the encoded software provided in the kit. The Applicant notes that Hacia does not teach or suggest this limitation, nor does this limitation appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, or Hoon alone or in combination.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.v. The Examiner's combination of references is missing the element of encrypting the results of a perioperative genomic profile with privacy security protocols (Claim 187)

In the Office Action of September 11, 2007 the Examiner notes:

> "In view of the newly presented rejection below over Lapointe, these arguments are moot." (Office Action of September 11, 2007, page 19.)

Accordingly, claim187 is addressed below.

II.A.1.w. The Examiner's combination of references is missing the element of decoding the results of a perioperative genomic profile with privacy security protocols (Claim 187)

In the Office Action of September 11, 2007 the Examiner notes:

"In view of the newly presented rejection below over Lapointe, these arguments are moot." (Office Action of September 11, 2007, page 19.)

Accordingly, claim 187 is addressed below.

II.A.1.x. The Examiner's combination of references is missing the element of selecting perioperative genomic profile markers by the criteria of analytical validity, clinical validity and clinical utility (Claim 189)

The Applicant respectfully notes that the Examiner's references both individually, and in combination, fail to teach all elements of claims 189, and claims that are dependent thereupon. The element of selecting perioperative genomic profile markers by the criteria of analytical validity, clinical validity and clinical utility does not appear in Miller, Quane, Acta, La Du, Pharmacogenetics, Evans, Poort, Hoon or Hacia. The Examiner has not indicated where this element is to be located in the Examiner's cited references.

In the Office Action of September 11, 2007 the Examiner notes:

"The ordinary artisan would have selected those markers, as discussed above, based upon these three criteria. Analyzing markers which have no utility or validity would not have been motivated by the art." (Office Action of September 11, 2007, page 19.) (Emphasis added.)

The Applicant respectfully disagrees. The Examiner's observations regarding missing elements in the claims are conclusory and unsupported by any evidence whatsoever. Moreover, the Examiner improperly responds to the fact of missing elements in the Examiner's combination of references with an argument based on the Examiner's speculation of what an ordinary artisan would or would not have been motivated to do.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.1.y. The Examiner's combination of references is missing the element of an integrated electronic system for organization of marker selection, subjecting a sample to an assay, and distributing the results of a patient's perioperative genomic profile (Claim 190)

In the Office Action of September 11, 2007 the Examiner notes:

"In view of the newly presented rejection below over Lapointe, these arguments are moot." (Office Action of September 11, 2007, page 20.)

Accordingly, claim 190 is addressed below.

II.A.2. The Examiner Provides no Motivation to Combine Miller in view of Quane or Acta and La Du or Pharmacogenetics and Evans or Poort, and further in view of Hoon and Hacia

In the Office Action of September 11, 2007 the Examiner makes numerous speculations regarding what an ordinary artisan would or would not have recognized, and what an ordinary artisan would or would not have been motivated to do. See, for example:

> "The ordinary artisan would have clearly recognized the benefit of testing an individual prior to surgery and subjection to the anesthesia for known genetic markers associated with a condition which was triggered by anesthetics." (Office Action of September 11, 2007, page 8.)

And:

> "The ordinary artisan would have been motivated to have screened individuals within two days prior to surgery to determine the genetic composition of the individuals to provide individualized diagnosis." (Office Action of September 11, 2007, page 9.)

And:

> "The ordinary artisan would have recognized that the art provides a large number of single nucleotide polymorphisms or other variations which are indicative of conditions." (Office Action of September 11, 2007, page 9.)

Despite these assertions, the Examiner has never provided any evidence of any kind to back up the Examiner's speculations. Similarly, despite the Applicant's multiple invitations to provide such evidence during prosecution of the present application, in the Office Action of September 11, 2007 the Examiner fails once again to do so.

The Applicant notes that the Examiner correctly identifies one of ordinary skill in the art as a clinician. Moreover, the Examiner expressly recognizes an anesthesiologist as one of ordinary skill in the art:

> "Combining more than one screening method to determine the genomic profile of a patient would have provided the anesthesiologist with a more complete picture or the patients genetic make-up." (Office Action of December 11, 2006, page 10.)

However, the Applicant submits that at the time the invention was made, ordinary anesthesiologists or other perioperative clinicians were not familiar with, and would not and did not look to the Examiner's non-analogous molecular biology references.

Morevoer, the Applicant submits that the Examiner's speculations and conclusory statements regarding the motivation of an ordinary artisan to combine the claim elements to yield the claimed invention are in error. The Examiner has failed to indicate where in the references cited, or elsewhere, there is such a suggestion of desirability to combine. The Examiner must provide a basis for combining alleged art references and their elements. Indeed, the requirement that the Examiner make a showing of a suggestion, teaching or motivation to combine the prior art references is "an essential evidentiary component of an obviousness holding."[1] The Applicant asks the Examiner to take note of the recent Supreme Court opinion which says that a specific showing by the Examiner is required:

> "Often, it will be necessary … to look to interrelated teachings of multiple patents … in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. See, *In re Kahn*, 441 F.3d 977, 988 (CA Fed. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness").[2]

In the office Action of September 11, 2007 the Examiner notes:

---

[1] *C.R. Bard, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998).
[2] *KSR v. Teleflex*, Slip Op No. 04-1350 (April 30, 2007).

> "The cited passage from KSR illustrates an analysis must be made specific, not that TSM is explicit. The analysis of KSR allows for a person with ordinary skill to have a good reason to pursue known options within his or her technical grasp." (Office Action of September 11, 2007, page 20.)

The Applicant submits that the Examiner's rejection has been neither specific, nor has the Examiner provided evidence that the claims of the present application were within the technical grasp of the anesthesiologist or perioperative caregiver of ordinary skill at the time the invention was made.

To the contrary, in the Declaration of Dr. Douglas Baird Coursin of June 10, 2007 Dr. Coursin explains that there was no suggestion or teaching in the prior art for the periperative genomic profiles of the presently claimed invention. Dr. Coursin notes:

> "The perioperative genomic profiles of the present patent application represent a completely novel approach that is not obvious in view of existing technologies. To my knowledge, no one previously proposed or disclosed perioperative genomic profiles that would be successful in screening a patient perioperatively to determine a risk for multiple complications during a surgical procedure." (Declaration of Dr. Coursin of June 10, 2007, page 2.)

In the Office Action of September 11, 2007 the Examiner fails to rebut or even to address this evidence in direct refutation of the Examiner's speculations. Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

The Examiner's cited references, the Examiners reference to the "the vast number of teachings, as exemplified by the extremely voluminous Information Disclosure Statement filed", and the Examiner's recognition of the desire to save lives, stand in stark contrast to the absence of anyone having come up with the invention prior to the filing of the present application. The Applicant notes that most of the references predate the filing of the application by many years. In view of all of this knowledge in the art, no one had

come up with the invention. The Examiner has not found a single anticipatory reference. Why is this?

Dr. Coursin's declaration provides an explanation. Dr. Coursin is one of the leading anesthesiologists in the country, and has been for many years. Dr. Coursin explains that skilled artisans, such as anesthesiologists, have as a primary mission to solve the problem solved by the present invention. Yet even with this long-felt need and years of searching by innumerable practitioners, no one solved this long-felt need using the approach of the present invention:

> ""However, if the perioperative genomic profiles of the present patent application were obvious, the ordinary practitioner would have arrived at the claimed combinations in view of long felt and unmet needs to directly identify genetic predispositions before, during and after surgery. No person having ordinary skill in the art, or even extraordinary skill, took this step before the claimed invention was made." (Declaration of Dr. Coursin of June 10, 2007, page 3.)

In the Office Action of September 11, 2007 the Examiner notes:

> "The declaration under 37 CFR 1.132 filed on June 14, 2007 is insufficient to overcome the rejection as set forth in the last Office action because: it is states that the claimed subject matter solved a problem that was long standing in the art. However, there is no showing that other so ordinary skill in the art were working on the problem and if so, for how long. In addition, there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would solve the problem. See MPEP 716.04. Here, the declaration of Dr. Coursin fails to provide evidence in the opinion declaration that the ordinary skilled artisans were working on the problem and for how long. Moreover, the declaration fails to provide any evidence that those working in the art on the problem knew of Quane, Miller, Acta Anaesthesiologica Scandinavica, La Du, Pharmacogenetics, Evans et al, Hoon et al, or Hacia references and were still unable to solve the problem. Thus,

the declaration is insufficient to overcome the 103 rejection of record." (Office Action of September 11, 2007, page 21.) (Emphasis in original.)

In this rejection the Examiner has made a number of errors. First, Dr Coursin's declaration clearly indicates that the problem solved by the present application was both long-standing, and an intense focus of the ordinary artisan's attention:

> "I have been in the practice of Anesthesiology and Critical Care Medicine for 26 years. During this entire time, and well before, the overriding mission of anesthesiologists, surgeons and other caregivers in the perioperative period has been to reduce the risk of adverse outcomes to the minimum for each patient. As well, it has long been recognized that inborn predispositions are significant contributors to morbidity and an mortality in the interval surrounding surgery. Despite this heightened level of vigilance, and intense focus on a shared mission, no one taught or suggested perioperative genomic profiles before the present patent application." (Declaration of Dr. Coursin of June 10, 2007, page2.)

Second, contrary to the Examiner's interpretation of MPEP 716.04, a demonstration of long-felt need does not require a showing that those working in the art on the problem knew of the Examiner's references. The Examiner has not indicated where this impression of the Examiner appears in MPEP 716.04. The Applicant notes that at the time the invention was made skilled artisans would not have looked, and did not look, to the Examiner's non-analogous literature. Moreover, even had they, the Examiner has never provided evidence that the skilled artisan would have known what to do with the non-analogous art to arrive at the various inventions now claimed. For example, the Examiner has never provided a reason why such a skilled artisan would have culled the Examiner's sub-set of references out of the thousands of references in the molecular biology art, let alone read them, understand them, and combinedd them in the specific manner proposed by the rejections.

Third, Dr. Coursin's declaration is not an "opinion declaration" as characterized by the Examiner, nor has the Examiner provided an interpretation of what the Examiner

believes is the definition of an "opinion declaration". Contrary to the Examiner's characterization, Dr. Coursin's declaration provides objective evidence of record that the Examiner has failed to rebut or even address in the Office Action of September 11, 2007. For example, Dr. Coursin's declaration factually describes the state of the art and the knowledge, capabilities, and actions of skilled artisans in the relevant time period.

In the Office Action of September 11, 2007 the Examiner notes:

> "As provided in MPEP 716.02(a) evidence must show unexpected results. The opinion declaration of Dr. Coursin does not appear to show any unexpected results." (Office Action of September 11, 2007, page 21.)

To the contrary, in the Declaration of June 10, 2007, Dr. Coursin explains that he himself has since used embodiments of the invention and achieved excellent, and unexpected, results:

> "In turn, a mean of 11 mutant alleles in aggregate (*i.e.*, homozygous plus heterozygous mutant polymorphisms) per patient were observed at loci comprising the perioperative genomic panel. These unexpected results demonstrate that significant genetic heterogeneity is present in most patients in advance of surgery that is not accounted for using contemporary tools for detection, *e.g.*, a family history check-box." (Declaration of Dr. Coursin of June 10, 2007, page 3.)

MPEP 716.02 states:

> "Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected." (MPEP 716.02)

The Applicants remind the Examiner that the standard for the presence or absence of motivation, long-felt need, and unexpected results does not apply to the expectations

of the Examiner in possession of the Application, but rather to the expectations of the ordinary artisan (*i.e.*, anesthesiologists and perioperative caregivers) at the time the invention was made. Clearly, Dr. Coursin's declaration provides evidence that the claims of the present application not only meet, but exceed these tests.

In a situation like the present one, there may be no better evidence of non-obviousness than the failure of an entire field to solve their primary problem, even with a wealth of information and technology known in the literature. The field failed to realize the solution because the solution was not obvious to these skilled artisans. These skilled artisans would not, and did not, see the combination the Examiner proposes they should have and would have seen. In the Office Action of September 11, 2007 the Examiner has failed to respond to these facts with contrary evidence.

The United States Patent and Trademark Office's rejection is based on hindsight knowledge of the invention wherein the Examiner has assumed what skilled artisans *should have* thought of the invention in view of numerous disparate pieces of prior art. In making the rejection, the Examiner, who is not one of skill in the art and who is in possession of hindsight knowledge of the invention, has *seen* an invention that the entire world of skilled artisans, focused for many years on the exact problem solved by the invention, had failed to see. Artisans, of ordinary and extraordinary skill in the field, who have devoted their careers to solving this problem, never put together the Examiner's combination of references, and never solved the problem. The only logical explanation is that the invention is non-obvious.

Notably missing from the Examiner's rejection is placement in the hands and minds of skilled artisans of: 1) the prior art of record (is this the type of work one skilled in the art would have reviewed in assessing the problem?); and 2) the mental and experimental process for modifying the art to arrive at the invention (even if they would have reviewed the cited art, would they have put the pieces together and modified the pieces appropriately?). At no point does the Examiner provide evidence of the handling of the references in the hands and minds of the appropriate skilled artisan. Regardless, even if the Examiner had done this, the evidence of long-felt but unresolved need demonstrates that skilled artisan did not, and would not, arrive at the invention. If it were obvious, they would have done it years before the filing of the present application.

Likewise, if it were obvious, Dr. Coursin and others who later employed the invention would not be surprised by the success of the invention at solving the problem.

Thus, the Examiner's references fail to establish *prima facie* obviousness of the claims. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.A.3. Claims 135-148 Are Not Obvious and Have Not Been Examined

In the Office Action of September 11, 2007 the Examiner has rejected claims 135-148 (See Office Action of September 11, 2007, page 1.) However, in the Office Action of September 11, 2007 the Examiner has not examined independent claims 135, 143 or 144, or claims dependent thereupon. Nowhere in the rejections are the elements of these claims addressed. Moreover, because Quane does not teach or suggest the genetic markers or conditions of claims 135 and 143, or the first marker in a first gene and a second marker in a second gene of claim 144, the Examiner has not, and cannot, point to Quane as a reference providing motivation to combine the elements of claims 135-148.

Thus, the Examiner has failed to establish *prima facie* obviousness of the claims 135-148. In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.B. Claim 185 Is Not Obvious

In the Office Action of September 11, 2007 the Examiner notes:

> "Therefore, it would have been prima facie obvious at the time the invention was made to have modified the detection methods of Miller, Quane, AAS, LaDu, Pharmacogenetics, Poort, Hoon and Hacia to encompass invader directed analysis as taught by Lyamichev." (Office Action of September 11, 2007, page 25.)

The Applicants respectfully disagree. Claim 185 depends upon claim 149 and is non-obvious for at least the same reasons that claim 149 is non-obvious. Moreover, the

Applicants submit that there is no motivation to combine the cited references in the manner suggested by the Office Action of September 11, 2007. As well, the Applicant submits that even if combined, there would be no expectation of success.

In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.C. Claims 151-160, 187-188, and 190 Are Not Obvious

In the Office Action of September 11, 2007 the Examiner notes:

> "Therefore, it would have been prima facie obvious at the time the invention was made to have designed a neural network as taught by Lapointe for the perioperative screening method of Miller, Quane, AAS, LaDu, Pharmacogenetics, Poort, Hoon and Hacia." (Office Action of September 11, 2007, page 24.)

The Applicants respectfully disagree. Claims 151-160, and 187-188 depend upon claim 149 and are non-obvious for at least the same reasons that claim 149 is non-obvious. As well, claim 190 depends upon claim 189 and is non-obvious for at least the same reasons claim 189 is non-obvious. Moreover, the Applicants submit that there is no motivation to combine the cited references in the manner suggested by the Office Action of September 11, 2007. For example, Lapointe does not teach or suggest characterization of DNA, nucleic acids, genetic testing, perioperative care or provide any teaching or suggestion to make the Examiner's combination of references. As well, the Applicant submits that even if combined, there would be no expectation of success.

In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.D. Claims 125 and 134 Are Not Obvious

The Applicants respectfully disagree. Claim 125 depends upon claim 106 and is non-obvious for at least the same reasons that claim 106 is non-obvious. Similarly, claim

134 depends upon claim 127 and is non-obvious for at least the same resaons that claim 127 is non-obvious. Moreover, the Applicants submit that there is no motivation to combine the cited references in the manner suggested by the Office Action of September 11, 2007. As well, the Applicant submits that even if combined, there would be no expectation of success.

In view of the above, the Applicant respectfully requests that this rejection be withdrawn.

II.E. Claims 125, 134, 160 and 186 Are Not New Matter

In the Office Action of September 11, 2007 the Examiner has rejected claims 125, 134, 160 and 186 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention." (Office Action of September 11, 2007, page 28).

In the Office Action of September 11, 2007 the Examiner notes:

> "The description does not support TNFalpha. The concept of markers within "TNFalpha" does not appear to be part of the originally filed invention. Therefore, "TNFalpha" constitutes new matter."

The Applicant respectfully disagrees. Explicit and ample support for TNFalpha may be found throughout the Specification at, for example:

> "Subjects carrying the TNF2 allele of the TNFα gene have an increased susceptibility to sepsis and death from sepsis after surgery (Mira, JAMA 282:561-568 [1999]). However, the only available assays measure cytokine production directly and are expensive, transient, and inconvenient. No conclusive, rapid screening assay for the presence of the TNF2 allele is available." (Specification page 2, line 30 to page 3, line 4.)

And:

"Examples include, but are not limited to markers for aminoglycoside ototoxicity, APOε4, wound cytokines, sepsis risk (TNFα), blood groups, coagulation factors, and thrombosis risk. In some embodiments, the perioperative screening assay includes other tests unrelated to the genomic profile for the main surgical application, but relevant in the case of a complication requiring emergency intervention (*e.g.*, blood typing)." (Specification, page 30, lines 5-9.)

And:

"In still further embodiments, markers predictive of possible complications during recovery from surgery, including, but not limited to, markers for a predisposition to sepsis (*e.g.*, TNF allele) are included. The TNF2 allele of TNFα is associated with an increased severity of sepsis. If a subject is found to have the TNF2 allele, intensive care monitoring post-surgery can be increased, decreasing the chance of death from sepsis. In addition, the practitioner may use the presence of the TNF2 allele as a factor in choosing a non-surgical treatment with a lower risk of sepsis." (Specification, page 34, lines 3-9.)

CONCLUSION

The Applicant believes that the pending claims should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: March 11, 2008

/David A. Casimir/

David A. Casimir
Registration No.: 42,395
CASIMIR & JONES SC
440 Science Drive, Suite 203
Madison WI 53711
(608) 218-6900